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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/803,566	03/18/2004	Andrew James Ratcliffe	USCA2206 US CNT	5977

5487 7590 08/29/2005

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EXAMINER

TUCKER, ZACHARY C

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 08/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

*HC*

## Office Action Summary

Application No.

10/803,566

Applicant(s)

RATCLIFFE ET AL.

Examiner

Zachary C. Tucker

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 June 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-9 is/are allowed.
- 6) ☒ Claim(s) 10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 March 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☒ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. herewith.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

***Response to Amendment***

As requested in the correspondence from applicants filed 24 June 2005 (hereinafter "present amendment"), which is in reply to the Office action mailed 24 June 2005 (hereinafter "previous Office action"), claims 1-8 and 10 have been amended and the title of the application has been amended. Abstract and specification at page 9 have also been amended as requested.

***Claim Rejections - 35 USC § 112***

In the previous Office action, claims 1-10 were rejected under 35 U.S.C. 112, second paragraph, for indefiniteness of the term "prodrug," as the molecular structures that are metabolized into compounds having the specified molecular formulae would not at once be apparent to a chemist of ordinary skill, and furthermore, because the identity of the prodrug compounds would be variable depending on the animal to which said prodrug was to be administered.

In view of the amendment to the instant claims (1-8), which changes "prodrugs" to "prodrug esters," the rejection is hereby withdrawn. Which types of esters of a compound according to the molecular structures in claims 1-8 would be metabolized into an active compound, that is, which esters of the claimed compound would serve as prodrugs, would easily be ascertainable by a chemist of ordinary skill in the art.

Claim 10 was found to be further indefinite because the scope of all diseases which are "capable of being modulated by JNK inhibition" is not known to those of ordinary skill. In view of the amendment to claim 10, which converts the claim to a method of inhibiting JNK activity in a patient, the rejection of claim 10 under 35 U.S.C. 112, second paragraph is hereby withdrawn.

Claims 1-10 were rejected in the previous Office action, under the first paragraph of 35 U.S.C. 112, for lack of an enabling disclosure for the full scope of all prodrugs of compounds according to the instant claims, and also therefore, for lack of enablement of the pharmaceutical composition comprised thereof and a method wherein said prodrugs are administered to a patient.

In view of the amendment to the instant claims whereby "prodrug" is changed to "prodrug esters," the rejection under 35 U.S.C. 112, first paragraph, is hereby withdrawn. A chemist of ordinary skill in the preparation of pharmaceuticals would not have to engage in an undue amount of experimentation to prepare prodrug esters of a compound according to the instant claims.

Also in the previous Office action, claims 1-10 were rejected under 35 U.S.C. 112, first paragraph, because the full scope of all solvates of the compounds according to the invention was deemed not enabled.

In view of the present amendment, the rejection is hereby withdrawn. Hydrates of the compounds according to the instant claims are not deemed to require an undue amount of experimentation to prepare. Water molecules, because of their small size, easily fill structural voids in crystal packing arrangements (Vippagunta et al, cited in the previous Office action, page 15, section #3). Since the "solvates" according to the claims are now limited to only one solvent, water, and the experimentation necessary to make the claimed hydrates would not be great.

Claim 10 was rejected in the previous Office action, for lack of enablement.

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Claim 10 has been amended, pursuant to the present amendment, in accordance with the examiner's suggestions. Upon review of the state of the art, the subject matter previously indicated as being allowable, a method of inhibiting JNK activity in a patient, with a compound according to claim 1, is recanted, with apologies for applicants for any confusion this erroneous indication of allowable subject matter may have caused.

Claim 10 is the subject of a new rejection under 35 U.S.C. 112, first paragraph, which follows.

***Title, Abstract and Specification***

Title, abstract and specification were objected to in the previous Office action.

In view of the present amendments to all three, the objections are hereby withdrawn.

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***New Claim Rejection - 35 USC § 112***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Upon review of the state of the art at the time the invention was made in JNK inhibition and compounds providing this effect, the following new rejection is deemed necessary.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The "how to use" portion of 35 U.S.C. 112, first paragraph, is not met by the disclosure with respect to instant claim 10. The claim reads on and embraces

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substantially all medical treatments, because of the recitation "in a patient." As applicants can appreciate, "patient" contemplates "one under medical treatment."

So, claim 10 is drawn to a method of practicing all medical treatments, and is therefore *prima facie* not enabled, because applicants have not taught how to use compounds of the invention for all medical treatments.

As evidence that JNK inhibitor compounds are certainly not viable treatments for all ailments, the examiner submits and directs applicants' attention to these references:

Harper and LoGrasso, "Inhibitors of the JNK Signaling Pathway" *Drugs of the Future*, vol. 26(10), pages 957-973 (2001).

and

Manning and Davis, "Targeting JNK for Therapeutic Benefit: From Junk to Gold?" *Nature*, vol. 2, pages 554-565 (July 2003).

The Manning and Davis reference was published after the invention was made, but is cited here because of its extensive bibliography of references which were published at the time the invention was made.

Harper and LoGrasso teach that JNK inhibitor compounds were being investigated for only *some* indications, particularly asthma and rheumatoid arthritis (page 968). Harper and LoGrasso is evidence that the scope of all medical treatments is not possible with JNK inhibitors.

It is self-evident that JNK inhibitors would not be sufficient to afford a means of achieving all medical treatments, as is required by instant claim 10's language.

***Allowable Subject Matter***

Claims 1-9 are allowed.

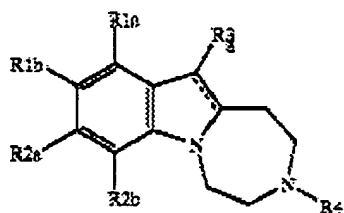
The following is an examiner's statement of reasons for allowance:

All rejections and objections are hereby withdrawn.

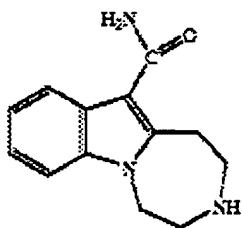
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The closest prior art, WO 01/72752 (Ennis et al), was summarized in the previous Office action, page 12.

Compounds disclosed in the Ennis et al publication have this general structure:



While the compound of example 12 in that publication has this structure –



So, the compounds from Ennis et al are quite similar – however, instant claim 1 does not permit for a phenyl ring being formed by joining R<sup>2</sup> and R<sup>3</sup>, and all of Ennis et al's compounds must have the tricyclic structure shown above. Additionally, the compounds of the Ennis et al publication are 5-HT (serotonin) receptor-affecting compounds, not JNK inhibitors. The Ennis et al publication exceeds 300 pages, so it has not been provided, because it does not serve as the basis for any claim rejection. Applicants most likely have access to the reference.

No disclosure in the prior art anticipates or renders obvious any of the compounds according to the invention, or a pharmaceutical composition comprising said compounds.

### **Conclusion**

Any inquiry concerning this communication should be directed to Zachary Tucker whose telephone number is (571) 272-0677. The examiner can normally be reached

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Tuesday-Thursday from 8:00am to 4:30pm or Monday from 6:00am to 1:30pm. If Attempts to reach the examiner are unsuccessful, contact the examiner's supervisor, James O. Wilson, at (571) 272-0661.

The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

zt

A handwritten signature in black ink, appearing to be "Zedman", written over the "zt" text.